V. Claim Amendments under 37 C.F.R. § 1.121

1. (Currently amended) A method of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces two peptides comprising Factor VII heavy chain and Factor VII light chain molecules.

2. (Currently amended) A method of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of [[said]] a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by SKI-1, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by SKI-1 produces two peptides comprising Factor VII heavy chain and Factor VII light chain molecules.

3. (Previously presented) A method according to claim 1, wherein said DNA vector further comprises a liver-specific promoter.

4. (Previously presented) A method according to claim 2, wherein said DNA vector further comprises a liver-specific promoter.

5. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acid 149 is changed from proline to arginine and amino acid 151 is changed from glycine to lysine.

6. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acids 147 through 150 have been replaced by the amino acid sequence of SEQ ID NO. 17.

7. (Previously presented) A method according to claim 5, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 2.

8. (Previously presented) A method according to claim 5, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 5.

9. (Previously presented) A method according to claim 5, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 7.

10. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acids 147 through 150 have been replaced by the amino acid sequence of SEQ ID NO. 18.

11. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic

cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acids 148 through 151 have been replaced by the amino acid sequence of SEQ ID NO. 17.

12. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acids 148 through 151 have been replaced by the amino acid sequence of SEQ ID NO. 18.

13. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acids 150 through 153 have been replaced by the amino acid sequence of SEQ ID NO. 17.

14. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acids 150 through 153 have been replaced by the amino acid sequence of SEQ ID NO. 18.

15. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acids 151 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 17.

16. (Currently amended) A method ~~according to claim 1~~ of promoting blood coagulation in an individual having a blood coagulation defect and in need thereof, comprising administering to the individual a blood coagulation enhancing effective amount of a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces Factor VII heavy chain and Factor VII light chain molecules, wherein amino acids 151 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 18.

17. (Canceled)

18. (Previously presented) A method according to claims 1 or 2, wherein enhanced blood clotting results in the individual relative to blood clotting when an effective amount of the DNA vector is not administered.

19. (Currently amended) A composition comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, [[and]] wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and, whereby cleavage by furin produces two peptides comprising Factor VII heavy chain and Factor VII light chain molecules.

20. (Currently amended) A composition comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by SKI-1, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII,[[and]] wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and whereby cleavage by SKI-1 produces two peptides comprising Factor VII heavy chain and Factor VII light chain molecules.

21. (Previously presented) A composition according to claim 19, wherein said DNA vector further comprises a liver-specific promoter.

22. (Previously presented) A composition according to claim 20, wherein said DNA vector further comprises a liver-specific promoter.

23. (Currently amended) A composition ~~according to claim 19~~ comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acid 149 is changed from proline to arginine and amino acid 151 is changed from glycine to lysine.

24. (Currently amended) A composition ~~according to claim 19~~ comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acids 147 through 150 have been replaced by the amino acid sequence of SEQ ID NO. 17.

25. (Previously presented) A composition according to claim 23, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 2.

26. (Previously presented) A composition according to claim 23, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 5.

27. (Previously presented) A composition according to claim 23, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 7.

28. (Currently amended) A composition ~~according to claim 19~~ comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acids 147 through 150 have been replaced by the amino acid sequence of SEQ ID NO. 18.

29. (Currently amended) A composition ~~according to claim 19~~comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acids 148 through 151 have been replaced by the amino acid sequence of SEQ ID NO. 17.

30. (Currently amended) A composition ~~according to claim 19~~ comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acids 148 through 151 have been replaced by the amino acid sequence of SEQ ID NO. 18.

31. (Currently amended) A composition ~~according to claim 19~~ comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acids 150 through 153 have been replaced by the amino acid sequence of SEQ ID NO. 17.

32. (Currently amended) A composition ~~according to claim 19~~ comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual,

said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acids 150 through 153 have been replaced by the amino acid sequence of SEQ ID NO. 18.

33. (Currently amended) A composition ~~according to claim 19~~ comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acids 151 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 17.

34. (Currently amended) A composition ~~according to claim 19~~ comprising a DNA vector encoding a human Factor VII polypeptide that can be converted to Factor VIIa when expressed in said individual, said Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII, wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site and, wherein amino acids 151 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 18.

35. (Canceled)

36. (Currently amended) An expression vector comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII,[[and]] wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and whereby cleavage by furin produces two peptides comprising Factor VII heavy chain and Factor VII light chain molecules.

37. (Currently amended) An expression vector comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by SKI-1, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII,[[and]] wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, and whereby cleavage by SKI-1 produces two peptides comprising Factor VII heavy chain and Factor VII light chain molecules.

38. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, wherein amino acid 149 is changed from proline to arginine and amino acid 151 is changed from glycine to lysine.

39. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, wherein amino acids 147 through 150 have been replaced by the amino acid sequence of SEQ ID NO. 17.

40. (Previously presented) An expression vector according to claim 38, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 2.

41. (Previously presented) An expression vector according to claim 38, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 5.

42. (Previously presented) An expression vector according to claim 38, wherein amino acids 147 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 7.

43. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, wherein amino acids 147 through 150 have been replaced by the amino acid sequence of SEQ ID NO. 18.

44. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have

been made in said area to create said enzymatic cleavage site, wherein amino acids 148 through 151 have been replaced by the amino acid sequence of SEQ ID NO. 17.

45. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, wherein amino acids 148 through 151 have been replaced by the amino acid sequence of SEQ ID NO. 18.

46. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, wherein amino acids 150 through 153 have been replaced by the amino acid sequence of SEQ ID NO. 17.

47. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, wherein amino acids 150 through 153 have been replaced by the amino acid sequence of SEQ ID NO. 18.

48. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, wherein amino acids 151 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 17.

49. (Currently amended) An expression vector ~~according to claim 36~~ comprising a nucleic acid sequence encoding a modified human Factor VII polypeptide comprising an enzymatic cleavage site susceptible to cleavage by furin, wherein said enzymatic cleavage site is located in the area of about amino acid 147 through about 154 of said Factor VII and wherein at least one amino acid mutations have been made in said area to create said enzymatic cleavage site, wherein amino acids 151 through 154 have been replaced by the amino acid sequence of SEQ ID NO. 18.

50. (Canceled)

51. (Previously presented) A composition according to claim 19, wherein said composition further comprises a pharmaceutically accepted carrier.

52. (Previously presented) A composition according to claim 20, wherein said composition further comprises a pharmaceutically accepted carrier.

VI. Conclusion

No fee is deemed necessary in connection with the filing of this communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 07-1074.

8/25/08
Date

Respectfully submitted,

Jennifer D. Tousignant
Attorney for Applicants
Registration No. 54,498
Telephone: (508) 270-2499
Facsimile: (508) 872-5415

GENZYME CORPORATION
15 Pleasant Street Connector
P.O. Box 9322
Framingham, Massachusetts 01701-9322